ABSTRACT

- **Title**

Postmarketing Surveillance Study for Kyprolis® (carfilzomib) in Korea (study number 20160117)

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- **Keywords**

Observational, carfilzomib, multicenter, effectiveness, safety.

- **Rationale and Background**

According to local regulation, a regulatory post-marketing surveillance (PMS) study is required for new medicines approved in Korea to collect safety and effectiveness data in routine clinical practice according to [Pharmaceutical Affairs Law] Article 32 and [Rules on Safety of Medicinal Product, etc.] Article 23 Paragraph 1.

Korea Risk Management Plan (K-RMP) of Kyprolis® includes this study as a part of the pharmacovigilance plan.

- **Research Question and Objectives**
    - Primary Objective: to determine the incidence of adverse events (AEs), serious adverse events (SAEs), and adverse drug reactions (ADRs) among patients with at least 1 prior therapy receiving Kyprolis® in real-life setting in its registered indication(s) as required by Ministry of Food and Drug Safety (MFDS).
    - Secondary Objective: to investigate effectiveness of Kyprolis® (overall response rate [ORR]).

- **Study Design**

This is a prospective observational study in post-marketing setting without a comparator arm.

- **Setting**

The study reviews the factors that are considered to affect the safety and effectiveness of patients with multiple myeloma who have received at least one prior therapy.

Inclusion criteria: patients receiving Kyprolis® for the first time during the re-examination period (31 March 2017 to 30 March 2023); consenting to participate in study and provide medical information.

Exclusion criteria: all contraindications specified in the local product information have to be considered. In addition, patients treated with any regimens not specified in the approved prescribing information of Kyprolis® in Korea or patients currently participating in another research study should be excluded.

Four hundred and sixty-four (464) patients were enrolled across 34 sites.

- **Subjects and Study Size, Including Dropouts**

The sample size was approximately 433 patients. Case report forms were collected from 464 subjects. Of the 464 subjects, 463 subjects (99.8%) were included in the safety analysis set for the primary objective and one subject (0.2%) was excluded from the safety evaluation as the subject did not receive carfilzomib.

A total of 421 subjects (90.7%) were included in the effectiveness analysis set for the secondary objective; 43 subjects (9.3%) were excluded from effectiveness analysis because there was no post-baseline effectiveness evaluation.

In this study, 275 subjects (59.4%) out of 463 subjects from the safety analysis set and 268 subjects (63.7%) out of 421 subjects from the effectiveness analysis set had long-term exposure to carfilzomib (subjects who received 6 doses of carfilzomib for twice-weekly Kyprolis® administration or 3 doses of carfilzomib for once-weekly Kyprolis® administration in Cycle 6).

- **Data Source(s) and Methods**

All data was extracted from information generated/gathered through routine medical practice. Each patient was followed-up on the first day of each cycle for the first 3 cycles following the initial visit, and then a follow-up visit at the end of study (EOS) visit (upon completion of Cycle 6 or 28 days from the last injection of Kyprolis®, whichever occurs first) per standard of care.

The AEs/ADRs were classified into 'expected' or 'unexpected' depending on whether they were listed in the local label.

- **Results**

Safety analysis: The period of this non-interventional study was from 31 March 2017 to 30 March 2023. Among the 463 subjects in the safety analysis set, 1432 AEs occurred in 388 subjects (83.8%). The incidence rate of ADRs was 38.7% (179 subjects) with 409 events, the incidence rate of SAEs was 27.2% (126 subjects) with 180 events, and the incidence rate of serious adverse drug reactions (SADRs) was 7.8% (36 subjects) with 49 events. The incidence rate of unexpected AEs was 39.3% (182 subjects) with 309 events and the incidence rate of unexpected ADRs was 8.0% (37 subjects) with 45 events. The incidence rate of fatal AEs was 3.7% (17 subjects) with 17 events and the incidence rate of fatal ADRs was 0.4% (2 subjects) with 2 events. The reported PTs for the fatal ADRs were cardiac failure and pneumonia with one event occurred in each subject (0.2%). The incidence rate of AEs leading to discontinuation of carfilzomib was 6.9% (32 subjects) with 35 events and the incidence rate of ADRs leading to discontinuation of carfilzomib was 3.2% (15 subjects) with 16 events.

The most frequent ADRs reported in 5% or more subjects (classified by preferred terms [PTs]) were neutrophil count decreased with 46 ADRs in 26 subjects (5.6%) and neutropenia with 36 ADRs in 27 subjects (5.8%). These events were listed in the label of Kyprolis® and the incidence of these events is consistent with the known safety profile of the product.

The most frequent unexpected ADRs (classified by PTs) were pancytopenia with 4 unexpected ADRs in 3 subjects (0.6%) and oedema with 3 unexpected ADRs in 3 subjects (0.6%). The incidence of these events is very low and does not result in the detection of any new risks for Kyprolis®.

Effectiveness analysis: In the effectiveness analysis set, a total of 290 subjects (68.9%) achieved overall response with mean time to response 2.22 ± 0.93 months at the time of Cycle 4 assessment; a total of 320 subjects (76.0%) achieved overall response with mean time to response 2.36 ± 1.18 months at the end of the study assessment.

Long term users: Among the 275 subjects in the long-term safety analysis set, 797 AEs occurred in 228 subjects (82.9%). The incidence rate of ADRs was 34.9% (96 subjects) with 204 events, the incidence rate of SAEs was 18.5% (51 subjects) with 64 events, and the incidence rate of SADRs was 5.5% (15 subjects) with 18 events. The incidence rate of fatal AEs was 0.4% (1 subject) with 1 event. The reported fatal AE was not

considered as an ADR. There were no AEs or ADRs leading to discontinuation of carfilzomib.

- **Discussion**

During the re-examination period (31 March 2017 to 30 March 2023), the evaluation of safety data did not result in the detection of any new risks for Kyprolis®. No new trends were detected when comparing to the previously reported safety data and no safety concerns were observed. The benefit-risk of carfilzomib continues to be positive when used for the approved indication.

- **Marketing Authorization Holder(s)**

Amgen Korea Limited

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